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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,117	12/29/2003	Derek O'Hagan	PP020038.0003	1746

27476 7590 07/24/2008

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EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
07/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,117	O'HAGAN, DEREK	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above claim(s) *2,17 and 29-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-16 and 18-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *2,17 and 29-85* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed February 15, 2008 is acknowledged and has been entered. Claims 1-85 are now pending in the present application.

2. Applicant's election without traverse of Group I, claims 1-28 and species meningitis B and phospholipid in the reply filed on April 16, 2007 is acknowledged. It is noted that claims 1, 3-16 and 18-28 read on the elected invention and species; these claims have been examined in the instant application.

3. Claims 2, 17 and 29-85 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and/or species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 16, 2007.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1, 3-16, 18, 19 and 22-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Hagan et al (WO 98/33487) taken with Hawkins et al (6290973).

O'Hagan et al teaches poly(lactide) or poly(lactide-co-glycolide) microparticles with adsorbed antigens (abstract). O'Hagan et al teaches "Particulate carriers with adsorbed or entrapped antigens have been used in an attempt to elicit adequate immune responses. Such carriers present multiple copies of a selected antigen to the immune system and promote trapping and retention of antigens in local lymph nodes. The particles can be phagocytosed by macrophages and can enhance antigen presentation through cytokine release. Examples of particulate carriers include those derived from polymethyl methacrylate polymers, as well as microparticles derived from poly(lactides) and poly(lactide-co-glycolides), known as PLG." (pp. 2-3; see also p. 7) O'Hagan et al teaches the use of microparticles with adsorbed antigens provides a safe and effective approach for enhancing the immunogenicity of a wide variety of antigens (p. 5). O'Hagan et al teaches that the microparticle has a diameter of about 100 nm to about 150 μm, more preferably about 200 nm to about 30 μm and most preferably about 500 nm to about 10 μm (p. 6). O'Hagan et al teaches the claimed immunogenic composition except for a synthetic phospholipid.

However, Hawkins et al teaches novel compounds that function as immunological adjuvants when co-administered with antigens (abstract; column 2, lines 10-13). Hawkins et al teaches the use of various synthetic phospholipids that can be used in vaccine compositions, pharmaceutical compositions or immunostimulatory compositions (cols. 3-7; cols. 187-188: ER804053, ER804057). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of O'Hagan et al with Hawkins et al to make an immunogenic composition comprising water, polymer microparticle, antigen adsorbed to microparticle and synthetic phospholipids (various phospholipids) for the purpose of immunizing a subject to increase or enhance immunogenic activity, immune response or stimulate/enhance protection against an infectious antigen for example. The claimed invention is prima facie obvious in view of the combined teachings of the prior art, absent any convincing evidence to the contrary.

7. Claims 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Hagan et al (WO 98/33487) taken with Hawkins et al (6290973) as applied to claims 1, 3-16,18, 19 and 22-28 above, and further in view of Muttilainen (Microbial Pathogenesis, 1995, 18:423-436) and Cox et al (Vaccine, 1997, 15/3:248-256).

O'Hagan et al and Hawkins et al have been described supra. O'Hagan et al and Hawkins et al teach the claimed invention except for the specific antigen, *Neisseria meningitidis* and meningitis B. However, Muttilainen et al teaches a composition comprising meningitis B antigen, the P1 protein, in a phospholipid vesicles or liposomes (abstract, methods and materials). Muttilainen et al teaches

the liposome formulation (P1 protein and liposomes) is good as an adjuvant (p. 432). Cox et al teaches that the "purpose of adjuvant combinations is to combine various adjuvant components to achieve the desired mix of immunological responses. The best-known adjuvant combination is Freund's complete adjuvant (FCA) which combines the immunomodulatory properties of ***Mycobacterium tuberculosis*** (essentially TDM and MDP) along with the short-term depot effect of w/o emulsions, This adjuvant generates very strong Thl and Th2 responses and is especially suited to hydrophilic immunogens. The Ciba-Geigy adjuvant formulation is a modification of FCA which uses a metabolizable oil (squalene) and nor-MDP. It has been used successfully in clinical trial. Despite the success of w/o formulations as a basis for adjuvant combinations (especially FCA and TiterMax) they do not normally induce CTL responses and require multiple doses for effective immunization i.e. long-term depots are not established." (p. 253) Cox et al teaches that "[L]iposomes offer a versatile formulation into which various immunomodulatory molecules can be incorporated. Examples include MPL, lipophilic MDP and Quil A. Although hydrophilic molecules can be incorporated within a liposome, the efficiency is generally low and liposome formulations are most suited for amphipathic immunogens. One other interesting combination is the mixture of MPL and QS21. Selection of the "best" adjuvant combination requires some knowledge of the chemical nature of the protective immunogen(s) and some idea of the nature of the immune response which is likely to be protective. However, even where knowledge of both these issues is minimal, rational selection of a small number of basic formulations and additives should permit selection of an effective adjuvant system. It is hoped that this review will help in this rational selection." (p. 253)

Barring any unexpected results and/or convincing evidence to the contrary, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of O'Hagan et al, taken with Hawkins et al, further in view of Muttilainen et al and Cox et al with a reasonable expectation of success to prepare the immunogenic composition as instantly claimed. Cox et al teaches that using a combination of adjuvants is desirable to achieve a mix of immunological responses.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method , and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to use combinations of adjuvants, which adjuvants are taught by Cox et al. Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-8975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. M. Minnifield/
Primary Examiner,
Art Unit 1645
July 20, 2008